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Considerations During Clinical Operation of Two Commercially Available Cryomachines

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Background and Objectives: Advances in the technology of cryomachines in the last 10 years have led to the development of both liquid nitrogen and argon-based Joule-Thompson cryomachines. Theoretical and practical evaluation of the CMS Accuprobe™ and the ENDOcare CRYOcare™ was performed as respective examples of these technologies.

Methods: Thermal gradients were calculated about both probes for the best case scenario of probe surface temperature equaling that of the cryogen used. Also, experimental evaluation in gelatin phantoms was performed with five probe arrays.

Results: Theoretically, a liquid nitrogen-cooled probe provides only a slight advantage over one cooled with liquid argon. However, the experimental performance evaluation demonstrated that the CRYOcare system creates an iceball faster with steeper internal temperature gradients than the Accuprobe. Further, temperature outputs from the Accuprobe were shown to be in error, likely due to the position of the thermocouple within the probe.

Conclusions: Cryomachine performance is determined more by technological innovations than by cryogen temperature. Thermocouple monitoring is urged for users of the Accuprobe.

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KEY WORDS: **cryosurgery; cryotherapy; thermocouple monitoring; thermodynamics; iceball**

INTRODUCTION

Cryosurgery, the practice of eradicating tissues by lethal freezing injury, is accomplished by cooling one or more metal probes which are in contact with the target tissue. The mechanisms of freezing injury that occur within the iceball, which forms about the probe, are complex and not fully understood [1–3]. The standard procedure, critical isotherm protocol cryosurgery, is performed under the assumption that sufficient necrosis has occurred once tissue has been enclosed by some critical isotherm [4]. The exact value of the critical temperature is not yet agreed upon but has been estimated to range from –20°C to –40°C [5–8]. Knowledge of the location of this critical isotherm is essential for effective treatment [9]. However, ultrasound, which is used to image iceball growth during a clinical procedure, cannot directly monitor temperature. In fact, the user is blind to everything beyond the near edge of the iceball due to the approximately 99% sonographic reflection at the ice interface [10]. Although temperature monitoring is possible at individual locations with thermocouples, it has not yet been

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universally accepted as part of the standard treatment procedure, even though such monitoring is recommended at the tumor edge to assure that the critical temperature has been reached [11]. The effectiveness of cryosurgery is dependent largely upon the ability of the surgeon to estimate the location of the critical isotherm given the location of the ice interface and temperature readings from thermocouples placed at strategic anatomic locations and in the cryoprobes themselves.

Unsubstantiated claims have been made regarding the performance of the Accuprobe™ and the CRYOcare™, two commercially available cryomachines. The manufacturer of the Accuprobe has claimed superior performance to the CRYOcare due to the use of a colder cryogen [12]. However, there has been no previous refereed publication comparing the performance of these two machines. This article evaluates the performance of the Accuprobe and the CRYOcare by observing the geometry of iceballs and their internal temperatures as functions of time. Further, the ability to predict temperatures within the iceball given probe temperature feedback from the two cryomachines is addressed.

MATERIALS AND METHODS

The performance of two commercially available cryomachines was evaluated both theoretically and practically. The Accuprobe, manufactured by Cryomedical Sciences (Rockville, MD), utilizes liquid nitrogen (LN_2) as a cryogen and can operate up to five cryoprobes simultaneously. High-pressure argon gas undergoing the Joule-Thompson effect is used to cool up to eight probes controlled by the CRYOcare unit manufactured by ENDOcare (Irvine, CA). All cryoprobes examined were 3.4 mm in diameter. Both machines were in good working order and were operated with the same physical parameters used clinically [e.g., time between LN_2 filling and operation (for the Accuprobe) and gas pressure (for the CRYOcare)]. Prior to experimentation, each probe tip was placed in saline and operated. Probes were visually inspected for gas leaks and iceball formation. No problems were noted.

During operation, the cryoprobes of both machines contain liquid cryogen as the argon liquefies upon expansion. On this basis, thermal gradients were calculated with the infinite cylinder solution of the Fourier heat equation for infinitely long cryoprobes with temperatures at the boiling point of each cryogen: –196°C for LN_2 and –186°C for argon. Although infinite cryoprobes are not used clinically, the infinite cylinder solution of the Fourier heat equation has been previously recommended as useful for determining the thermal gradient near the midplane of the cryoprobe normal to the probe itself [13]. Gradients for both temperature probes were calculated within ice tubes, the iceball shape produced about infinite probes, extending 15 mm beyond the cryoprobe surface.

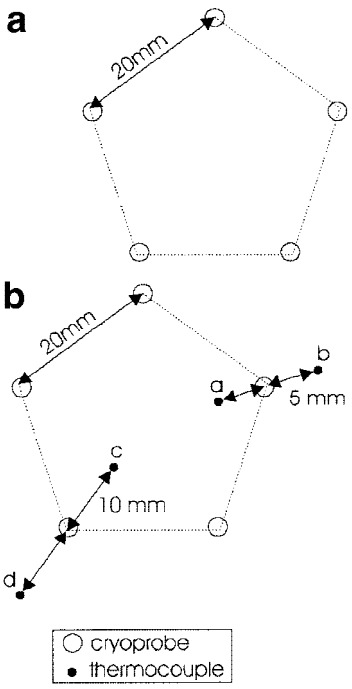

Fig. 1. **(a)** The pentagonal configuration of cryoprobes and **(b)** the location of thermocouples about the probes

Two experimental trials were performed. The first consisted of a visual side-by-side evaluation of the iceballs created by the two machines and was performed in a gelatin phantom (1.4% gelatin initially at room temperature). New and virgin probes were arranged in a pentagonal configuration, with each probe separated by 2.0 cm (Fig. 1a). The flow of cryogen from both machines was initiated at the same time. Photographs were taken at several times during the formation of the iceballs.

In a separate trial, using the same probe configuration with new and virgin probes, two pairs of T-type thermocouples (Omega Engineering, Laval, Quebec, Canada) were used to record temperatures in the iceball. Surrounding one of the cryoprobes in the configuration a pair of thermocouples was placed, one 5 mm toward the center and one 5 mm away from the center of the pentagon. Around a second cryoprobe a pair of thermocouples was placed in a similar pattern 10 mm from the center of the cryoprobe (Fig. 1b).

Both machines provide real-time probe temperature outputs, as observed by thermocouples placed inside the probe during the manufacturing process. Temperature readings are usually fed into the cryomachines and displayed on a screen during the procedure. These readings were redirected to an OMB DAQBOOK thermal acquisition system (Omega Engineering), which recorded temperatures along with temperature readings of the four thermocouples once every second.

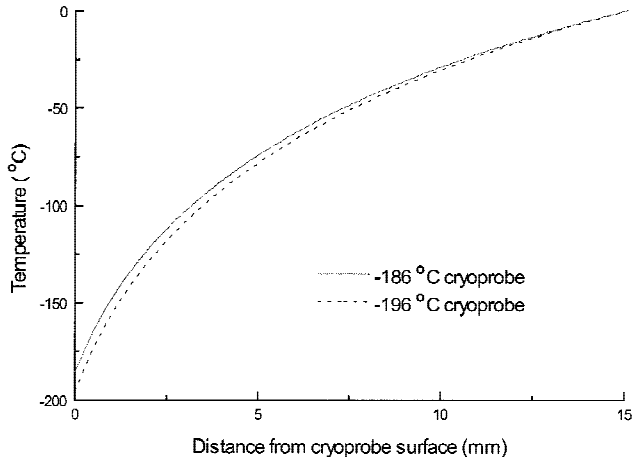

Fig. 2. Theoretical thermal gradients about infinitely long 1.7 mm radius cryoprobes with surface temperatures of –196°C (liquid nitrogen) and –186°C (liquid argon).

RESULTS

Figure 2 shows the thermal gradients that would be produced inside the ice tubes formed about a single infinitely long cryoprobe. The two curves represent best case theoretical scenarios in which the outer surface of the probes are at the boiling temperature of the cryogen used: –196°C for LN_2 and –186°C for argon.

Figure 3 shows iceballs during the side-by-side comparison at 1, 5 and 15 min, respectively. In all photographs, the Accuprobe is on the left and the CRYOcare is on the right.

Temperature recordings from the two pairs of thermocouples placed 5 mm and 10 mm from the probe centers are displayed in Figure 4. During the second experiment, temperature readings from a thermocouple located within each of the five cryoprobes were recorded. Figure 5a represents the thermal histories of the five Accuprobes as recorded by their internal thermocouples. The temperatures recorded by the ENDOcare probes are presented in Figure 5b.

DISCUSSION

For critical isotherm protocol cryosurgery, the volume of necrotic tissue is assumed to be the volume enclosed by the critical isotherm. This is a function of the depth of the critical isotherm in the iceball. Figure 2 shows the theoretical gradients resulting from infinitely long cryoprobes with surface temperatures of LN_2 and liquid argon. Using these theoretically calculated gradients, the locations of sample critical isotherms of –20°C and –40°C were obtained (Table I). The difference in the radial location of the sample critical isotherm resulting from a probe temperature difference of 10°C is, at most, 0.3 mm. Although multiple probes are usually used clinically, these temperature gradients for an infinitely long single cryoprobe illustrate the small effect a 10°C difference in probe temperature has on the surrounding thermal gradients. On this theoretical basis, the LN_2-based Accuprobe should perform slightly better than the argon-based CRYOcare.

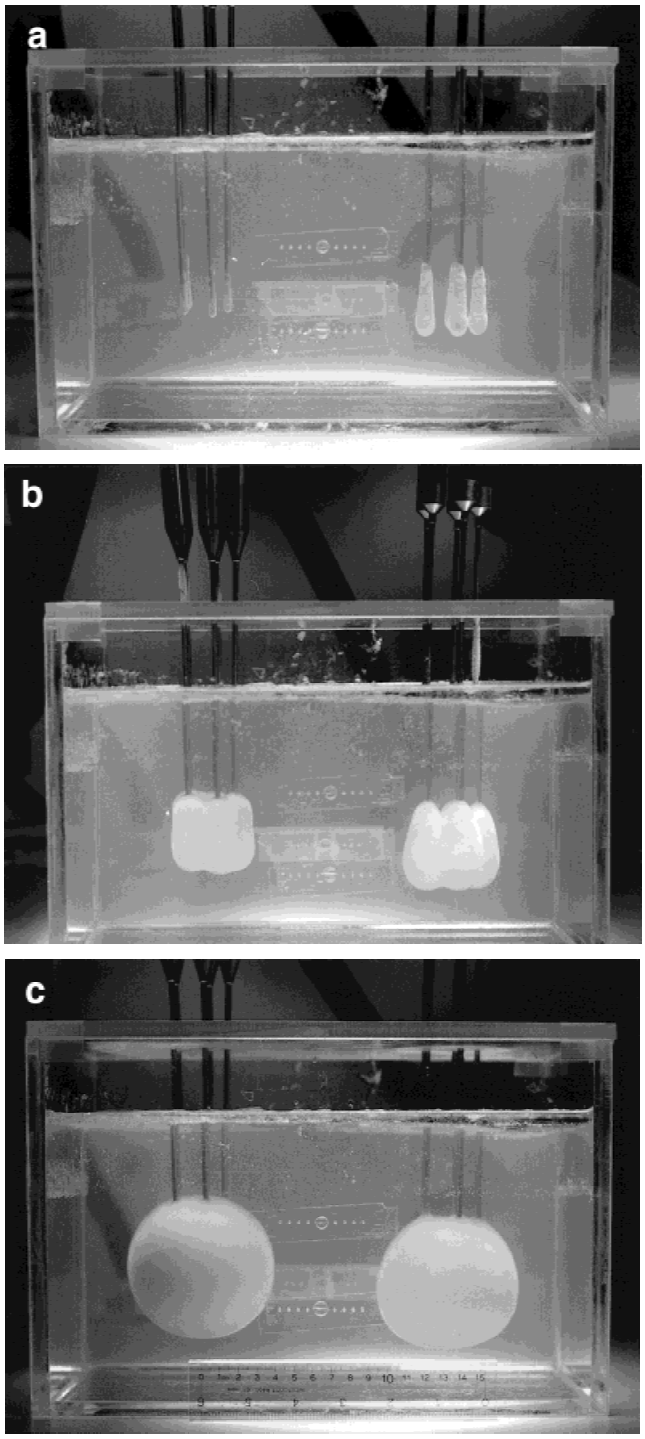

Fig. 3. Photographs taken at **(a)** 1 min, **(b)** 5 min, and **(c)** 15 min after the initiation of cryogen flow during the side-by-side comparison. The Accuprobe is on the left and the CRYOcare is on the right in each photograph.

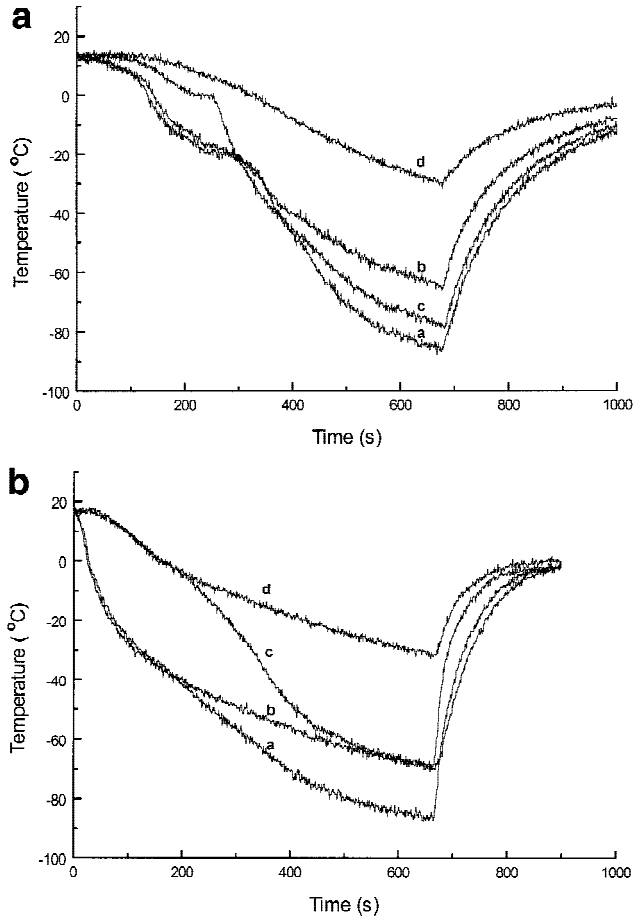

Fig. 4. Temperatures recorded at the four thermocouple locations (a–d), which are shown in Figure 1, for **(a)** the Accuprobe and **(b)** the CRYOcare.

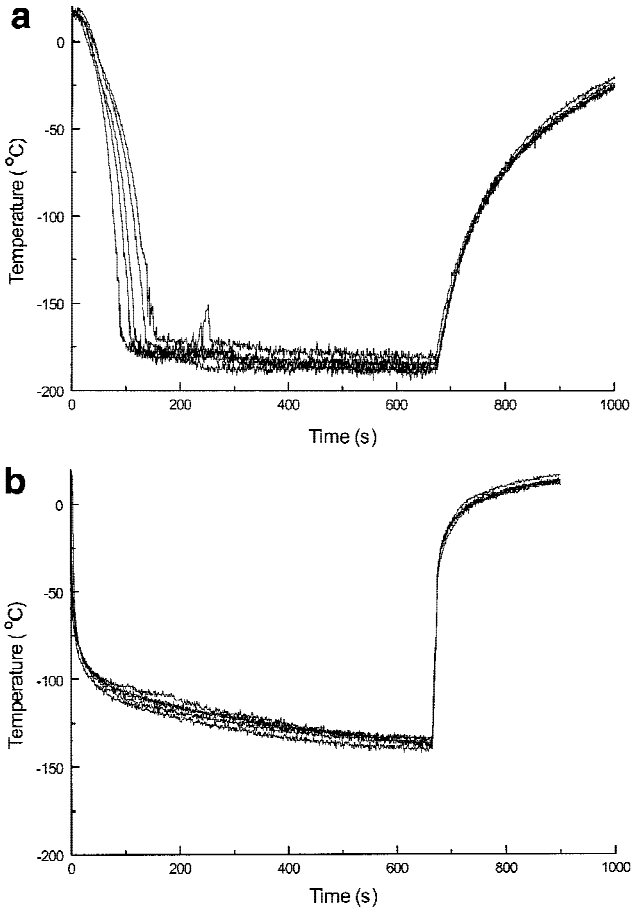

Fig. 5. Temperature readings from the thermocouples located within the five cryoprobes during the second experiment for **(a)** the Accuprobe and **(b)** the CRYOcare.

The above evaluation is based on the assumption that the temperature of the surface of the cryoprobe tip is the same as the boiling point of the cryogen used. However, this is not the case. In fact, the liquid does not actually touch the inner surface of the probe's outer casing inside either probe. There is a gas envelope between the liquid and the inner probe surface. (A similar phenomenon is a drop of water dancing on a hot grill, where it is separated from the grill by a layer of water vapor). Thus, it is problematic to determine the actual temperature of the cryoprobe surface. However, by observing the geometry of the iceballs formed and the temperatures within them, it is possible to infer probe performance characteristics.

Figure 3a illustrates that the CRYOcare forms ice about its probes much faster than the Accuprobe. In fact, this is a significant advantage of the Joule-Thompson cryomachines over LN_2-based machines. The response time to both the freeze and thaw computer commands is less than 1 sec for the CRYOcare compared to a minimum of 30 sec for the Accuprobe. Since oscillating probe temperatures have been shown to potentially enhance the lethality of an iceball [14], fast probe temperature response is important. Thermal cycles with a period on the order of 20 sec are required for this enhanced lethality, but this cycle period is not possible with LN_2 cryomachines. The equilibrium iceballs formed by the two machines are about the same size but slightly different in shape (Fig. 2c). The Accuprobe iceball is closer to a spherical shape compared to the teardrop shape of the iceball made by the CRYOcare. A teardrop-shaped iceball is closer to the actual geometry of the prostate gland and allows for a more conformal therapy.

TABLE I. Location of Sample Critical Temperatures of −20°C and −40°C Based on Gradients Calculated With the Infinite Cylinder Approximation

	−196°C (nitrogen)	−186°C (argon)
−20°C	11.7	11.4
−40°C	8.8	8.6

The qualitative observation of faster iceball formation with the CRYOcare is further supported by the quanti-

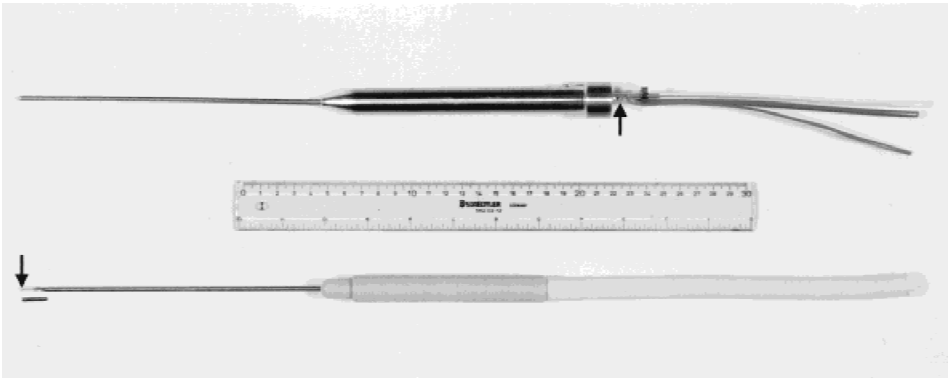

Fig. 6. Dissected cryoprobes: the Accuprobe **(top)** and the CRYOcare **(bottom)**. Arrows indicate the location of the internal thermocouples.

tative observations of temperatures recorded from the cryoprobes during their operation (Fig. 4a,b). The temperature gradient of the Accuprobe was lower during the initial formation of the iceball (the first 5 min), but the temperature of the four monitored points around the Accuprobe subsequently caught up during the ensuing 5 min. After 10 min, the length of a typical freeze during a clinical procedure, the temperatures of the four points were very similar for the iceballs produced by the two machines.

These observations are the opposite of what one might expect given the temperature readings of the thermocouples within the cryoprobes as displayed on the screen of each cryomachine. Figure 5a and b shows that the Accuprobe reports much lower temperatures from its probe thermocouple than the CRYOcare. On this basis, an operator would expect not only faster iceball formation by the Accuprobe, which was not observed, but also a much steeper thermal gradient within the iceball formed by the Accuprobe compared to the CRYOcare. This is not supported by the data in Figure 4a and b, and the difference in displayed temperature readings between the probes is likely due to the difference in thermocouple location within the cryoprobes. Figure 6a and b shows an Accuprobe and a CRYOcare cryoprobe, respectively, dissected to display the actual thermocouple locations. The thermocouple in the CRYOcare cryoprobe is located at the tip of the cryoprobe, while the thermocouple in the Accuprobe is soldered to the vent where cryogen exits the probe after visiting the probe tip. This location is over 33 cm (13 inches) from the tip, whose temperature it is claimed to represent. Users of the Accuprobe would be prudent to not consider the probe temperature reading as accurate. These observations coincide with our clinical experience with the Accuprobe, where we have easily removed probes from patients when the probe temperature was reading –30°C or lower. Our institution has previously recommended the use of thermocouple monitoring during any cryosurgical procedure [11]. Based on the present data, thermocouple monitoring is essential when using the Accuprobe not only to ensure that the critical temperature has been reached at the tumor edge but also to gain accurate knowledge of the probe performance. Relying on the probe temperature outputs to predict temperatures around cryoprobes is not recommended. The temperatures displayed correspond to the location of the thermocouple junction and do not represent, or necessarily correlate, to that of the tip surface temperature.

CONCLUSION

Cryomachine performance is determined more by the technology of the machine itself rather than by the temperature of the cryogen it employs. Clinical decisions regarding the location of the critical isotherm based upon temperature readings from thermocouples located within the cryoprobes are not recommended. Users of the Accuprobe are especially cautioned in this respect since probe temperature readings do not accurately reflect cryoprobe surface temperature or performance. The need for thermocouple monitoring at strategic locations, such as the tumor margin, is reinforced.

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